NASA TECHNICAL TRANSLATION NASA TT F-15,393

CHANGES IN THE GAS METABOLISM, GAS HOMEOSTASIS AND TISSUE RESPIRATION IN THE RAT DURING PROLONGED HYPOKINESIS

V. L. Popkov, E. S. Mailyan, Yu. S. Galushko,
Ye. A. Kovalenko, Ye. I. Zaytseva, I. A. Nitochkina,
L. V. Smulova and A. V. Ryazhskiy

Translation of: "Izmeneniya gazoobmena, gazobogo gomeostaza i tkanevogo dykhaniya u krys pri dlitel'noy gipokinezii," Fiziologichnoy Zhurnal SSSR im. I. M. Sechenova, Volume 56, Number 12, 1970, pp. 1808-1812

(NASA-TT-F-15393) CHANGES IN THE GAS METABOLISM, GAS HOMEOSTASIS AND TISSUE RESPIRATION IN THE RAT DURING PROLONGED HYPOLINESIS (Techtran Corp.) 11 p HC $4.00 CSCL 06C G3/04

N74-16824

Unclas 30405

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
WASHINGTON, D. C. 20546 FEBRUARY 1974

STANDARD TITLE PAGE

1. Report No. NASA TT F-15,393	2. Government Accession No.	3. Recipient's Catalog No.
4. Title and Subtitle CHANGES IN THE GAS METABOLISM, GAS HOMEOSTASIS AND TISSUE RESPIRATION IN THE RAT DURING PROLONGED HYPOKINESIS		5. Report Date FEBRUARY 1974 6. Performing Organization Code
7. Author(s) V. L. Popkov, E. S. Mailyan, Yu. S. Galushko, Ye. A. Kovalenko, Ye. I. Zaytseva, I. A. Nitochkina, L. V. Smulova and A. V. Ryazhskiy		8. Performing Organization Report No. 10. Work Unit No.
9. Performing Organization Name and Address Techtran Corporation P.O. Box 729 Glen Burnie, Maryland 21061		11. Contract or Grant No. NASw-2485 13. Type of Report and Period Covered Translation
12. Sponsoring Agency Name and Address NATIONAL AERONAUTICS AND SPACE ADMINISTRATION WASHINGTON, D. C. 20546		14. Sponsoring Agency Code

15. Supplementary Notes

Translation of: "Izmeneniya gazoobmena, gazobogo gomeostaza i tkanevogo dykhaniya u krys pri dlitel'noy gipokinezii," Fiziologichniy Zhurnal SSSR im I. M. Sechenova, Volume 56, Number 12, 1970, pp. 1808-1812.

16. Abstract

Among the white rats kept in confining cages to limit motor activity of the animals, the overall gas metabolism and intratissue gas homeostasis did not significantl change over the course of the 60--day long experiment period. However the intensity of respiration of certain tissues change: in the liver it increased, in the myocardium it decreased. The physical working capacity underwent a five-fold decrease. The 60-day long period of hypokinesis caused retarded growth of the animals.

17. Key Words (Selected by Author(s))	18. Distribution Statement		
	Unclassified-Unlimited		
19. Security Classif. (of this report)	20. Security Classif. (of this page)	21. No. of Pages	22. Price
Unclassified	Unclassified	9	

NASA-HQ

CHANGES IN THE GAS METABOLISM, GAS HOMEOSTASIS AND TISSUE RESPIRATION IN THE RAT DURING PROLONGED HYPOKINESIS

V. L. Popkov, E. S. Mailyan, Yu. S. Galushko,
Ye. A. Kovalenko, Ye. I. Zaytseva, I. A. Nitochkina,
L. V. Smulova and A. V. Ryazhski,

Limitation of the motor activity of man is one of the most important prob- /1808* lems of our time. The latter is linked with the progressively growing decrease in the volume of muscular work in all spheres of labor, and the course of scientific and technical progress. The effect of hypokinesis on the organism is also of interest for clinical practice and space medicine.

In the many investigations devoted to general phenomenology and pathogenesis of hypokinesis, a significant amount of attention is paid to the gas--energetic aspect of hypokinesis [1-4, 8, 9]. This is due to the fact that a decrease in the level of functioning of the muscular system must unavoidably alter the level of the energetic processes in the tissues, which in its turn has a direct link with the gas metabolism and with the dynamics of gases at all levels of transport of O_2 and CO_2 in the organism.

The task of this investigation was a complex study of overall gas metabolism, intratissue gas homeostasis and the intensity of tissue respiration in white rats kept in a condition of long term (60 days) hypokinesis.

The Method

Limitation of motor activities of the subject animals was caused by placing white rats in special restricting cages where they were kept under conditions of fixed posture for a period of 60 days. The construction of the cell made it possible in the process of the experiment to feed and water the animals and to remove waste products. The subject and control rats were kept in one room under identical temperature conditions (+18-+20°); feeding of both groups of animals was carried out according to a diet of the Institute of

*Numbers in the margin indicate pagination in the foreign text.

Nutrition, USSR Academy of Medical Sciences. As opposed to the test animals, the control animals were placed in groups of 10 in cages of the ordinary vivarium type measuring 45 X 45 X 35 cm. The overall gas metabolism was determined by the closed chamber method using 48 test and 30 control animals. For this purpose the group of rats (8-10) was placed for 1 hour in a sealed chamber measuring 0.17 m^2 volume at a temperature of +20°. The average sum consumption of oxygen, liberated carbon dioxide gas (in ml per 100 g living weight per minute) and the respiratory coefficient (R.Q.) were determined according to the final chemical composition of the air (in %).

The intratissue oxygen tension (pO_2) and carbon dioxide gas tension (pCO_2) were determined after the tissue depot [11] method in the modification of V. L. Popkov. The method of gas tonometry used by us is based on the physical law of Henry-Dalton: the tension of gases dissolved in the tissue is equal to the tension of these gases located in a closed space above the tissue (in the gas depot). Constant gas depots in the subcutaneous tissue was created by means of subcutaneously administering 20 cm^3 air. After 18 hours, 2-3 cm^3 air evenly mixed with the tissue gaseous mixture was drawn off by means of a hypodermic needle for microanalysis on the Scolender apparatus. The percentage composition of the gaseous mixture was calculated for oxygen tension (pO_2) and carbon dioxide gas tension (pCO_2) in mm Hg, with calculation of common atmospheric pressure; the vapor pressure of water (pH_2O) and the temperature of the gaseous medium mixture in the depot were determined. /1809

The intensity of tissue respiration was determined at the 45th and 60th days of hypokinesis using the Warburg apparatus in sections of tissue of the cerebral cortex, the heart, the liver, and the skeletal muscles (quadraceps muscle of the hip). The incubation of sections was carried out in a Wringer--Lock solution in an atmosphere of pure oxygen [10].

At the end of the 60-day long experiments, in both groups of animals (test and control), determination was made of the maximum physical working capacity tested by maximum swimming time of rats under a load equal to 15% of the animal's weight (maximum dynamic work), and according to maximum time the animal could stay in a vertical seat with transverse straps (maximum static

work). The relationship of free and phosphorylation oxidation (according to amytal-resistant and amytal-sensitive respiration) was studied by means of intraabdominal administration of sodium-amytal in the amount of 7 mg per 100 g animal weight (after the method of S. P. Maslov and I. N. Ivashkina [5]).

Results of the Investigation and Their Discussion

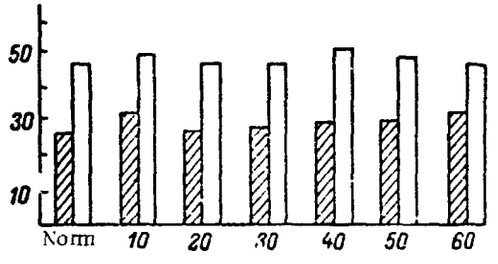
The investigations showed that common gas metabolism among white rats over a period of a continuous 60-day long stay in cages providing limited movement did not significantly change. As one can see from the average data cited in Table 1, no significant differences in oxygen consumption in the course of the experiment were found among the test and control rats. The liberation of carbon dioxide gas among the test rats somewhat exceeded that of the control animal, which led to higher values of the respiratory coefficient, but this difference was statistically unreliable.

TABLE 1. GENERAL GAS METABOLISM AMONG WHITE RATS DURING 60-DAY LONG HYPOKINESIS

Day of the experiment	Control rats				Test rats			
	No. of animals	Average consumption of O_2 in ml/100 g weight/1 min	Average liberation of CO_2 per ml/100 g weight/1 min	Respiratory coefficient	No. of animals	Average consumption of O_2 in ml/100 g weight/1 min	Average liberation of CO_2 ml/100 g weight/1 min	Respiratory coefficient
Starting gas metabolism	30	3.10	2.18	0.72	48	3.03	2.08	0.68
15th	30	2.97	2.32	0.78	48	3.11	2.64	0.84
30th	30	3.27	2.28	0.69	46	3.24	2.68	0.82
45th	30	2.91	2.12	0.72	39	3.11	2.65	0.84
60th	30	2.83	2.43	0.85	23	2.98	2.66	0.89

In addition to determining the general gas metabolism, the indices of intratissue gas homeostasis – pO_2 and pCO_2 were studied (according to the gas depots method). Detention of oxygen in the tissues is a terminal stage of the oxygen cascade along the path of passage of O_2 into the organism, while tissue tension of carbon dioxide gas characterizes the initial stage of CO_2 diffusion from the organism into the environment. The gaseous composition of the tissues exerts a large influence on the work of enzymes and, consequently, on the course of metabolic processes in the tissues of the organism. As one can see from the drawing, the absolute values of pO_2 and pCO_2 in the subcutaneous gas depots

during hypokinesis did not significantly change. An analysis of our experimental data, after Student, showed that fluctuations in pO_2 and pCO_2 in the tissues throughout the course of the experiment did not extend beyond the limits of a /1810 reliable interval ($\bar{x} \pm 1.96\ \sigma_{\bar{x}}$) for the original level; differences in the values of pO_2 and pCO_2 in the test and control animals were also not noted ($p > 0.10$). In our opinion, fluctuations in the intratissue pO_2 and pCO_2 are linked with the ordinary rhythm of vital activity of the organism. Since the absolute value of pO_2 and pCO_2 in the peripheral tissues is a terminal result of the coordinated activity of the respiratory, circulatory, and other systems of the organism, then proceeding from the obtained data it should be concluded that the system of oxygen and carbon dioxide gas transport in the organism does not change during hypokinesis.



Tissue Tension of Oxygen (pO_2) and Carbon Dioxide Gas (pCO_2) in mm Hg in the Norm and During Hypokinesis. Along the axis of the ordinate — tissue tension of oxygen and carbon dioxide in mm^3. White column — pCO_2; striped column — pO_2.

In addition to the general gas metabolism, determining the consumption of oxygen by certain tissues is of interest. A study of the intensity of tissue respiration (on 34 rats) showed that among the tissues investigated by us the most clearcut changes appear in the liver and the myocardium (Table 2). Thus, the consumption of O_2 in slides of the liver at the 45th day of hypokinesis increased to 131 ± 9.97 mm^3 per 100 mg moist tissue per hour at 85 ± 5.98 mm^3 in the control group ($p < 0.0001$). By the 60th day this increase in respiration became less pronounced and was 108 ± 11.1 mm^3 O_2 ($p > 0.05$). In the myocardium, opposite results were obtained. Here, after only 45 days, a tendency toward a decrease in absorption of O_2 was detected, and on the 60th day of hypokinesi there was a significant, statistically reliable weakening of respiration (38 ± 6.22 mm^3 per 100 mg per moist tissue per hour with 62 ± 4.78 in the control, $p < 0.05$). In the brain tissues and tissues of the skeletal muscles, after 45 and 60 days from the onset of hypokinesis, no clearcut changes in the intensity of respiration were ob ved.

TABLE 2. INTENSITY OF TISSUE RESPIRATION IN mm^3 O_2 PER 100 mg MOIST TISSUE PER HOUR

Conditions of the experiment		Brain	Heart	Liver	Muscles
Control	*M*	78	62	85	19
	m	±4.25	±4.78	±5.98	±3.98
	n	17	17	17	17
Hypokinesis 45 days	*M*	85	56	131	25
	m	±7.25	±7.95	±9.97	±6.59
	n	12	12	1[illegible]	12
	p	> 0.05	> 0.05	< 0.0001	> 0.05
Hypokinesis 60 days	*M*	65	38	108	17
	m	±5.72	±6.22	±11.1	±4.30
	n	5	5	5	5
	p	> 0.05	< 0.05	> 0.05	> 0.05

In the later investigations carried out on pulp samples of tissues incubated in a medium containing oxidation substrates (succinate and α-ketoglutarate), the same principles were obtained. In the liver tissue, the intensity of respiration increased; in one experiment by 50% (30th day of hypokinesis), and in the other by 63% (45th day of hypokinesis, $p < 0.05$). In the tissues of the myocardium absorption of O_2 decreased by 17%, $p < 0.05$ (60th day). /1811

Hence, the repeat experiments with long term limited movement showed that in the course of the second month of hypokinesis periods of an increase in the intensity of respiration in the liver occur with decrease of its level in the myocardium.

In addition to studying the general and regional gas metabolisms, the energetic effectiveness of respiration estimated according to the amytal test was carried out. However no differences were found in the percentage relationship of amytal-resistant and amytal-sensitive respiration at the 60th day of hypokinesis. Consequently, the relationship of free and phosphorylation oxidation in the investigated periods of time among the test animals remain the same as in the control. Amytal-resistant respiration among the test rats comprised 46 ± 2.0%, in the control — 45 ± 1.8%.

The dynamics of live weight of the test and control animals is shown in Table 3, from which it follows that the weight of the test rats constantly lags behind the weight of the control. By the end of the 60th day of the experiment, the weight of the control rats, which were kept under conditions of free movement, was 392 + [sic] 18 g, significantly exceeding the weight of the test rats — 273 ± 10 g.

After a 60-day long period of hypokinesis, there was a sharp decrease in the animals' physical endurance (Table 4). Changes in both the dynamic and static component of working capacity were noted. The duration of maximum dynamic work decreased by more than 2.5 times. There was an even greater decrease in the capacity for static work (a decrease of 9 times). These data indicate far progressing detraining of the animals' skeletal musculature in the course of the 60-day long period of hypokinesis.

TABLE 3. WEIGHT OF WHITE RATS DURING A 60-DAY LONG PERIOD OF HYPOKINESIS

Day of the experiment	Control rats		Test rats	
	No. of animals	Weight of animal, in g ($\bar{x} \pm \sigma_{\bar{x}}$)	No. of animals	Weight of animal, in g ($\bar{x} \pm \sigma_{\bar{x}}$)
Original weight	30	274 ±15	48	254 ± 8
15	30	323 ±12	48	255 ± 6
30	30	348 ±16	46	261 ±10
45	30	380 ±18	39	272 ± 5
60	30	392 ±18	23	273 ±10

TABLE 4. MAXIMUM PHYSICAL WORKING CAPACITY OF WHITE RATS DURING A 60-DAY LONG PERIOD OF HYPOKINESIS

Physical endurance	Control animals	Animals after a 60-day long period of hypokinesis
Maximum duration of maximum dynamic work (swimming test) in seconds ($\bar{x} \pm \sigma_{\bar{x}}$)	191 ±0.37	76 ±0.10
Maximum duration of maximum static work (vertical posture) in seconds ($\bar{x} \pm \sigma_{\bar{x}}$)	183 ±0 57	20 ±0.02

Hence, the investigations which were conducted showed that a 60-day long /1812
period of hypokinesis does not cause significant changes in the general gas metabolism in tension of oxygen and carbon dioxide in the tissues. However, respiration of certain tissues changes: in the course of the second month periods of increased intensity of respiration of the liver and a decrease of respiration in the myocardium were detected. With respect to the reasons for these changes, one can surmise that an increase in respiration of the liver cells were probably caused by a predominance of catabolic processes over anabolic ones [6] in this period of hypokinesis. But the load level of respiration of the cardiac muscles is related to the training of the myocardium with the transition of it to a new and lower level of functioning under conditions of lowered motor activity.

The sharpest disruptions in our tests were observed in the functional activity of the skeletal musculature (sharp decrease in working capacity) and in the physical development of the animals, which was manifested in a decrease in tempos of weight increase of the animals. The lag in weight of the animals indicates disorders of the plastic metabolism and is caused, obviously, by disorders of protein synthesis [7].

Conclusions

1. A 60-day long period of hypokinesis does not have a significant influence on the general gas metabolism and intratissue gas homeostasis.

2. Long term hypokinesis causes changes in the intensity of tissue respiration: an increase of respiration in the liver and a decrease in the myocardium (at the 45th and 60th days).

3. Physical working capacity of the animals after a 60-day long period of hypokinesis decreases several times.

4. A 60-day long period of hypokinesis causes a significant retardation in increase in the animals' weight.

REFERENCES

1. Balakhovskiy, I. S., L. I. Karpova and S. F. Simpura, *Probl. kosmichesk. biolog.*, Vol. 1, p. 345, 1962.
2. Ivanov, D. I., V. B. Malkin, I. N. Chernyakov, V. L. Popkov and Ye. O. Popova, in the book: *Aviatsionnaya i kosmicheskaya meditsina* [Aviation and Space Medicine], Moscow, p. 202, 1963.
3. Kalinichenko, I. R., in the book: *Mater. nauchn. konfer. molodykh spetsialistov, posv. pamyati A. V. Lebedinskogo* [Materials of a Scientific Conference of Young Specialists Devoted to the Memory of A. V. Lebedinskiy], Moscow, p. 95, 1965.
4. Katkovskiy, V. S., *Kosmichesk. biolog. i med.*, Vol. 1, p. 67, 1967.
5. Maslov, S. P. and I. N. Ivashkina, *Vopr. med. khimii*, Vol 10, p. 24.
6. Fedorov, I. V., V. N. Vinogradov, Yu. I. Milov and L. A. Grishanina, *Kosmichesk. biolog. i med.*, Vol. 1, p. 53, 1967.
7. Fedorov, I. V., Yu. I. Milov, V. N. Vinogradov and L. A. Grisnanina, *Kosmichesk. biolog. i med.*, Vol. 2, p. 22, 1968.
8. Deitrick, J. E., G. D. Whedon and E. Shorr, *Am. J. Med.*, Vol. 41, p. 3, 1948.
9. Taylor, H. L., D. Henschel, J. Brozek and A. Keys, *J. Appl. Physiol.*, Vol. 2, No. 5, p. 223, 1949.
10. Umbreit, W. W., R. H. Burris and J. F. Stauffer, *Manometric Techniques and Related Methods for the Study of Tissue Metabolism*, Minneapolis, 1946.
11. Van Liew, H., *J. Appl. Physiol.*, Vol. 17, No. 6, p. 851, 1962.

Translated for the National Aeronautics and Space Administration under Contract No. NASw-2485 by Techtran Corporation, P.O. Box 729, Glen Burnie, Maryland, 21061; translator, Samuel D. Blalock, Jr.